

ENHANCED TRANSPORT USING MEMBRANE DISRUPTIVE AGENTS

Abstract of the Invention

5 Compositions and methods for transport or release of therapeutic
and diagnostic agents or metabolites or other analytes from cells, compartments
within cells, or through cell layers or barriers are described. The compositions
include a membrane barrier transport enhancing agent and are usually
administered in combination with an enhancer and/or exposure to stimuli to
10 effect disruption or altered permeability, transport or release. In a preferred
embodiment, the compositions include compounds which disrupt endosomal
membranes in response to the low pH in the endosomes but which are relatively
inactive toward cell membranes (at physiologic pH, but can become active
toward cell membranes if the environment is acidified below ca. pH 6.8),
15 coupled directly or indirectly to a therapeutic or diagnostic agent. Other
disruptive agents can also be used, responsive to stimuli and/or enhancers other
than pH, such as light, electrical stimuli, electromagnetic stimuli, ultrasound,
temperature, or combinations thereof. The compounds can be coupled by ionic,
covalent or H bonds to an agent to be delivered or to a ligand which forms a
20 complex with the agent to be delivered. Agents to be delivered can be
therapeutic and/or diagnostic agents. Treatments which enhance delivery such
as ultrasound, iontophoresis, and/or electrophoresis can also be used with the
disrupting agents.